Original Article

Vitamin D Status in Children Diagnosed with Pulmonary Tuberculosis: Hospital-Based Prospective Evaluation (February–October 2025)

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Abstract

Background: Tuberculosis (TB) remains a significant source of childhood morbidity and mortality in nations with a high TB burden, such as India, which contributes approximately one-quarter of all TB cases worldwide. Vitamin D is a significant nutrient that helps the body fight Mycobacterium tuberculosis by affecting both innate and adaptive immunity. The association between low vitamin D levels and active TB is tested through observational studies, although limited research exists on children in India. Purpose: (1) to determine the serum level of 25-hydroxyvitamin D [25(OH)D] in children with pulmonary tuberculosis; (2) to determine the prevalence of vitamin D deficiency and insufficiency; and (3) to clarify whether there is a correlation between the level of vitamin D and the clinical/radiological severity of pulmonary TB. **Material and Methods:** This hospital-based prospective observational study was conducted between February 4, 2025, and October 31, 2025, at the Departments of Paediatrics and Respiratory Medicine at Al Falah Medical College and Hospital. Thirty children aged 1 to 14 years were recruited in consecutive order and were newly diagnosed with pulmonary TB according to the recommendation of the national TB program. Their demographic information, nutritional conditions, clinical presentation, contact history, and radiographic images were captured. A chemiluminescent immunoassay was used to measure serum 25(OH)D. According to the Indian Academy of Pediatrics (IAP) cut-offs, vitamin D deficiency, insufficiency, and sufficiency were defined as <12 ng/mL, 12-20 ng/mL, and >20 ng/mL, respectively. The severity of diseases (mild, moderate, severe) was determined by clinical burden of symptoms, radiographic (extent), and microbiological (confirmation) aspects. Descriptive statistics were used to analyze the data, and the chi-square test and Student t-test were used; a p-value of less than 0.05 was considered significant. **Results:** The mean age of the participants was 8.1 3.2 years, and 16 (53.3%) were boys. The total prevalence rate of vitamin D deficiency was 18 (60%), insufficiency 7 (23.3), and only 5 (16.7) had an enough amount of vitamin D. Children under-nourished (BMI-for-age below-2 SD) were prevalent in 17 (56.7) children and more frequent in children with vitamin D deficiency than in those with adequate levels (72.2% vs 33.3%; p=0.04). The proportion of moderate-to-severe pulmonary TB was 20 (66.7%; p=.02), and it was also strongly correlated with vitamin D deficiency: 15/18 (83.3%; 5) deficient and 5/12 (41.7%; 58.3%) non-deficient children showed moderate-to-severe TB. Those with moderate-to-severe disease had lower mean serum 25(OH)D levels (11.5 4.2 ng/mL) than those with mild disease (17.0 3.8 ng/mL; p=0.002). **Conclusion:** Among children in this hospital-based group with TB of the pulmonary type, a high prevalence of low levels of vitamin D was demonstrated. Under-nutrition and more serious illness were strongly associated with vitamin D deficiency. The results of this study indicate that regular testing of vitamin D status should be considered as a potential additional measure in the management of pediatric pulmonary TB, with appropriate correction. It is worth noting, though, that the trials have conflicting results in clinical use.

Keywords: Vitamin D, 25-hydroxyvitamin D, pulmonary tuberculosis, children, hypovitaminosis D, under-nutrition, India.

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Introduction

Tuberculosis is one of the principal infectious diseases that causes morbidity and mortality in the world today. The recent global TB report indicates that the worldwide number of TB incidents in 2010 was between 10 and 11 million, with 1 million deaths, with a significant share of 10-12 per cent of children and young adolescents experiencing TB. India alone is noted to have the largest segment of the global burden of TB, with an estimated 26 per cent of the annual incidents.[1,2] The National TB Elimination Programme is one of the efforts, yet India alone is recorded to absorb the biggest share of the global burden of TB. Although childhood TB is often the paucibacillary type, which is less contagious than the adult one, it is the sentinel indicator of recent spread in the community. It reflects a shortcoming of case detection and prevention efforts.[1,3]

Children lack fully developed immune responses, are malnourished, and may have underlying diseases, making them more susceptible to the progression of infection into disease.[1,4,5] Vitamin D has received particular interest due to its role as a

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determinant of tuberculosis risk and outcomes, which are known to be influenced by vitamin D deficiency, as well as by vitamin and protein deficiencies and undernutrition.[5-10]

Vitamin D promotes innate immunity by activating vitamin D-dependent pathways during M. tuberculosis binding to toll-like receptors, effectively enhancing intracellular killing and phagolysosomal fusion.[6,11-17] Vitamin D may also decrease excessive inflammation and modulate adaptive immunity by promoting the activation of vitamin D-dependent pathways on the binding of M. tuberculosis to toll-like receptors that enhance the killing by macrophages and epithelial cell phagocytosis.

Several studies and reviews done among adults have indicated that patients with active TB tend to have lower serum 25(OH)D when compared to healthy patients. This deficiency has been associated with increased risk of disease in the case of children.[4,7,13] In children, there is limited information, although it has generally corroborated this observation. Case-control studies and meta-analyses have reported that 25(OH)D levels are significantly lower in children with TB or latent TB infection than in controls. [8-10] Indian studies have also found that the rate of low vitamin D is high among children with TB, but varies between regions, ages, and seasons.

Vitamin D deficiency and insufficiency are prevalent amongst healthy Indian children. This has resulted from factors such as dark skin, lack of outdoor activities, urbanization, air pollution, and an insufficient diet. Huge bodies of evidence imply that fifty to seventy percent of Indian kids and adolescents have low 25(OH)D concentrations.[7,11] The IAP has proposed certain objectives with deficiency being less than 12 ng/mL, insufficiency being 12-20 ng/mL, and adequacy being greater than 20 ng/mL, and also recommends supplementation.[11,12]

There are varied outcomes of interventional trials on vitamin D supplementation for tuberculosis (TB). There is little evidence of the clinical benefits of vitamin D in pediatric TB. However, there are small benefits in sputum conversion or immune marker levels, and other studies show no benefit.[4,13,14] The role of vitamin D in TB in children, particularly in high-transmission locations in India, is under investigation. Additional local data are needed to determine the vitamin D levels in children with pulmonary TB and their impact on disease severity and nutrition.

This research was performed at the Al Falah Medical College and Hospital and had the following objectives; (1) to measure the serum 25(OH)D levels of children with pulmonary TB; (2) to assess the prevalence of vitamin D deficiency and insufficiency based on the IAP cut-offs; (3) to explore the relationship between vitamin D status and clinical/radiological symptoms severity and nutritional status of this group.

Materials and Methods

Study design and setting

This was a prospective, observational study conducted in the Departments of Paediatrics and Respiratory Medicine at Al Falah College of Medicine and Hospital, a teaching institution serving an urban and rural community. The study period was from 4 February 2025 to 31 October 2025. It encompassed cooler and monsoon days and seasons, which may influence the amount of sunlight penetrating the skin and generating vitamin D.

Study population: All children aged between 1 and 14 years were identified as having newly diagnosed pulmonary TB and were either visiting the paediatric outpatient department or admitted to the paediatric ward, as they were included in the study. The 30 children who met the inclusion and exclusion criteria were recruited with the written consent of their parents or guardians, and older children provided age-appropriate consent.

Inclusion criteria

Age 1 to 14 years.

Incidentally, based on national TB program regulations, diagnosis of pulmonary TB will involve one or more of the following:

- Recurrent coughing and/or fever longer than 2 weeks, loss or non-thriving, tiredness.
- Chest X-ray with possible TB inflammation, i.e., hilar lymphadenopathy, segmental or lobar consolidation, cavitation, or miliary.
- Microbiological confirmation by sputum smear, cartridge-based nucleic acid amplification test (CBNAAT), where possible, by culture.
- History of intimacy with an infectious TB victim, and an encouraging clinical or radiological presentation.

Exclusion criteria

- History of the TB disease or anti-tubercular medication in the past.
- Chronic liver, kidney disease, or malabsorption disorders are known.
  - The use of systemic corticosteroid therapy or an enzyme-inducing anticonvulsant in the long run.
- Known disorders that necessitate the use of vitamin D supplementation, e.g., active childhood rickets, which is of an active nutritional nature.

The children who were below 18 years old and whose parents/guardians did not provide consent.

Sample size

We have chosen a sample size of 30 children based on the number of pediatric pulmonary TB cases likely to occur over the next 9 months and logistical constraints. Past research in India has revealed that TB-unaffected children are vitamin D-deficient between 50 and 75 percent. With 30 subjects, we were able to accurately estimate this prevalence and identify simple correlations with disease severity and nutritional status.

Data collection

We collected with the help of a structured form: Demographic information, such as age, sex, and place of residence (urban or rural).

- Socioeconomic status, which is put on a standard scale.
- TB history, such as BCG vaccination status (scarred or unscarred), family TB contact in the recent (two years) period, and past diseases.
- Clinical, including cough time, fever, willpower loss, not hungry, night sweats, the production of blood during coughs, and breathlessness.

Anthropometry was measured (weight, height or length, and mid-top arm circumference) using calibrated instruments. To assess the extent of under-nutrition in the population, we determined BMI-for-age z-scores based on WHO growth standards and defined a BMI-for-age score below -2 SD as a manifestation of under-nutrition.

Chest radiographs were reviewed by a radiologist and a pediatric pulmonologist who were unaware of vitamin D levels. Radiological severity, as was categorized in the US, was:

- Mild: lymphadenopathy of the hilum, which is unilateral, and colloquial lesions of the lungs.

Moderate bilateral lymphadenopathy, no cavitation, segmental or lobar formation, moderate pleural effusion.

Cavitary disease, miliary pattern, large bilateral consolidation, or large pleural effusion is severely absent.

As appropriate, we analyzed sputum or gastric aspirates using smear microscopy and/or CBNAAT. Microbiological confirmation was also documented, but it is not necessary to include it, as bacilli are less common in pediatric TB.

Operational definitions

- Vitamin D status: We reported the serum 25(OH)D concentrations as per IAP as deficient (below 12 ng/mL), insufficient (12 to 20 ng/mL), and sufficient (over 20 ng/mL).

Disease severity: We have adopted a combined classification of severity, developed on a case-by-case basis, based on clinical factors (symptom duration, weight loss, respiratory distress), radiological and microbiological confirmations, to classify patients as mild, moderate, or severe pulmonary TB. For analysis, we would tend to combine moderate and severe cases as moderately severe disease.

Laboratory methods

At enrolment, we collected 3 and 5 mL of venous blood, before any future vitamin D supplementation that may be recommended as a standard treatment. We divided the serum and put it at 2-8 °C till analysis. Serum 25(OH)D levels were estimated in batches using a chemiluminescent immunoassay, with internal and external quality control processes. The inter-assay coefficient of variation had been less than one in ten.

We performed routine investigations, including complete blood count, erythrocyte sedimentation rate, C-reactive protein, and liver and kidney function tests, as it was necessary in clinical practice, and reported the results when possible.

Statistical analysis: We entered the data into a spreadsheet and analyzed them using the standard statistical package SPSS. This is because continuous variables were summarized as mean ± standard deviation (SD) or median (interquartile range), depending on the distribution, whereas categorical variables were summarized as frequencies and percentages. A Student t-test was used to compare mild and moderate-to-severe disease between the two groups for continuous variables. The chi-square test or Fisher's exact test was employed to assess the association between categorical variables (such as vitamin D deficiency vs. non-deficiency and disease or nutritional condition severity) according to the methods used. We believed that a p-value below 0.05 was of importance.

Ethical considerations: Al Falah Medical College and Hospital received approval for the study protocol from the Institutional Ethics Committee. The parents or legal guardians of all participants provided written informed consent, and children aged seven and above provided assent in accordance with institutional policy. We held the privacy of patient information.

Results

Baseline characteristics: Thirty children who had just been diagnosed with pulmonary TB were recruited. The average age was 8.1, and the difference between the maximum and minimum ages was 14 years (2 and 14 years, respectively). The age of children comprised six (20%) between the ages of 1-4 years, 12 (40%) between the ages of 5-9 years, and 12 (40%) between the ages of 10-14 years. There were 16 boys (53.3%) and 14 girls (46.7%).

Seventeen (56.7%) children were undernourished (BMI-for-age <−2 SD), and the remaining 13 (43.3%) children were in a normal state of nutrition. A history of household TB contact during the last two years was found in 11 (36.7) children. A BCG scar was reported in 24 (80%) of the group.

Cough, fever, weight loss, and reduced appetite were the most common presenting complaints, reported 28 times (93.3%), 26 times (86.7%), 22 times (73.3%), and 21 times (70%), respectively. Respiratory distress was observed in 9 (30) children.

Radiographically, 9 (30%) children were mildly diseased, 13 (43.3%) were moderate, and 8 (26.7%) were severe. In 11 (36.7%) participants, microbiological confirmation (smear and/or CBNAAT-positive) was achieved.

Table 1: Baseline characteristics of children with pulmonary tuberculosis (n=30)

Variable	Category	n (%)
Age group (years)	1–4	6 (20.0)
	5–9	12 (40.0)
	10–14	12 (40.0)
Sex	Male	16 (53.3)
	Female	14 (46.7)
Nutritional status (BMI-for-age)	Normal (≥−2 SD)	13 (43.3)
	Under-nourished (<−2 SD)	17 (56.7)
TB contact history	Present	11 (36.7)
	Absent	19 (63.3)
BCG scar	Present	24 (80.0)
	Absent	6 (20.0)
Radiological severity	Mild	9 (30.0)
	Moderate	13 (43.3)

	Severe	8 (26.7)
Microbiological confirmation	Yes	11 (36.7)
	No	19 (63.3)

Vitamin D status: The mean serum 25(OH)D level in the cohort was 13.8 ± 4.9 ng/mL (range 6.2–25.6 ng/mL). Using IAP cut-offs, 18 (60%) children were vitamin D deficient (<12 ng/mL), 7 (23.3%) insufficient (12–20 ng/mL) and, only 5 (16.7%) sufficient (>20 ng/mL).

Table 2: Distribution of serum vitamin D status in children with pulmonary TB (n=30)

Vitamin D status	Serum 25(OH)D (ng/mL)	n (%)
Deficient	<12	18 (60.0)
Insufficient	12–20	7 (23.3)
Sufficient	>20	5 (16.7)
Total	—	30 (100)

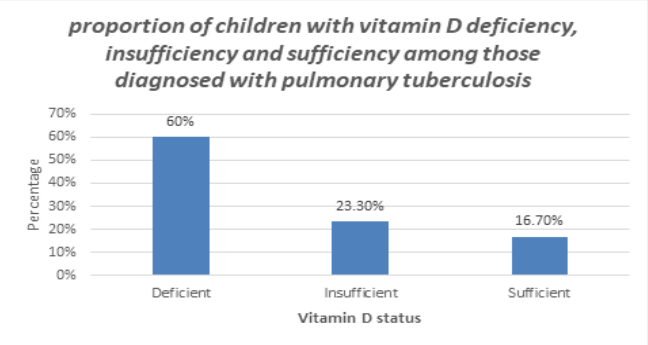

Figure 1: Bar chart showing the proportion of children with vitamin D deficiency, insufficiency and sufficiency among those diagnosed with pulmonary tuberculosis (n=30).

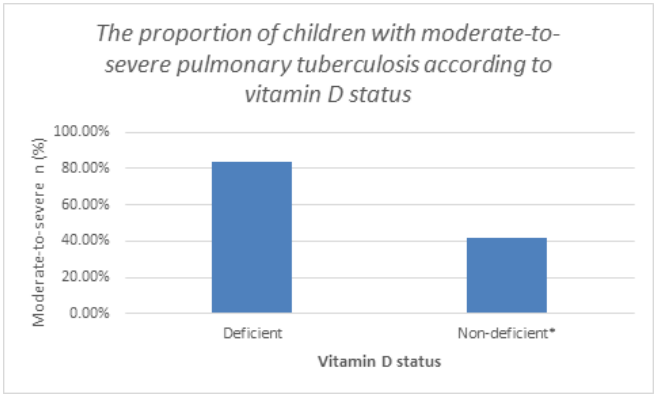

Figure 2: Clustered bar chart showing the proportion of children with moderate-to-severe pulmonary tuberculosis according to vitamin D status (deficient vs non-deficient).

Correlation of vitamin D status and disease severity.
Among children with disease severity analysed by vitamin D status, 15 of 18 (83.3%) vitamin D-deficient children had moderate-severe pulmonary TB, compared with 5 of 12 (41.7%) who were not vitamin D-deficient (inadequate or adequate). This was found to be statistically significant (χ^2 = 5.65; p = 0.02).
The average level of serum 25(OH)D in the mild all sick children was 17.0 ± 3.8 ng/mL, and that of moderate-to-severe all sick children was very low (11.5 ± 4.2 ng/mL; p = 0.002).

Association between vitamin D status and nutritional status: Of children (n=17) who were undernourished, 13 (76.5%) were deficient in vitamin D, 3 (17.6%) were insufficient, and only 1(5.9%) was adequate. Conversely, 5 (38.5), 4 (30.8), and 4 (30.8) of the children in normal nutritional status (n=13) were deficient, insufficient, and sufficient, respectively. Undernourished children showed a higher prevalence of the vitamin deficiency (p=0.04).

Table 3: Association of vitamin D status with disease severity (n=30)

Vitamin D status	Mild disease n (%)	Moderate-to-severe n (%)	Total n (%)
Deficient	3 (16.7)	15 (83.3)	18 (100)
Non-deficient*	6 (50.0)	6 (50.0)	12 (100)
Total	9 (30.0)	21 (70.0)	30 (100)

*Non-deficient = insufficient + sufficient.

Table 4: Relationship between vitamin D deficiency and under-nutrition (n=30)

Nutritional status	Vitamin D deficient n (%)	Non-deficient n (%)	Total n (%)
Under-nourished	13 (76.5)	4 (23.5)	17 (100)
Normal	5 (38.5)	8 (61.5)	13 (100)
Total	18 (60.0)	12 (40.0)	30 (100)

Other clinical associations: Children who were deficient in vitamin D had a longer mean time to symptom onset (6.4 2.1 weeks) than those who were not deficient (5.1 1.8 weeks). However, this difference was not statistically significant (p=0.08). Also, no significant difference in the prevalence of microbiological confirmation was found between the deficient and non-deficient groups (8/18 vs 3/12; p=0.71).

Discussion

This prospective study was conducted in a hospital, and its prevalence rate indicates that many children with pulmonary

tuberculosis have low vitamin D levels. Based on IAP levels, 60% of respondents were vitamin D deficient, and another 23.3% were inadequate. Only a quarter of children were well endowed with vitamin D. Vitamin D deficiency was associated with under-nutrition and increased clinical and radiological severity of pulmonary TB.

Comparison and contrast with another research: Our observations are consistent with those of other researchers in India and elsewhere who report that their children with low vitamin D levels have TB. Kashyap et al. discovered that in children with TB, approximately three-quarters of children with TB had low vitamin D levels, and the median 25(OH)D of patients was substantially lower than that of the control children.<|human|>Kashyap et al. have observed that children with TB and low vitamin D levels were found, and the median of 25(OH)D in a patient was significantly lower than in control children. In India, other studies have also reported high prevalence of low vitamin D in pediatric TB, among other studies with lower rates of 25(OH)D in the children compared to the non-TB children.[9,18,19]

Venturini et al. noted in their study that, across the globe, Vitamin D levels were found to be inadequate or deficient in almost half of children in a multicentre cohort, independent of TB status. This demonstrates that low vitamin D levels are common even in areas with low TB incidence.[10] Meta-analyses suggest that adults and children with TB are more likely to have lower 25(OH)D levels than controls. Still, the effect size differs across body regions, depending on the study method.[7,13]

Our rate of 60 percent vitamin D deficiency in children with TB is a higher rate than that reported by community studies of child vitamin D deficiency and insufficiency of 58-70 percent of children and adolescents in India.[7,11,12] This indicates that children with TB are even a particularly risky group in an already at-risk population.

Our correlation coefficient for vitamin D deficiency and moderate-to-severe pulmonary TB is significant. Children with a deficient state were far more prone to a large volume of radiological sickness and lower mean 25(OH)D levels as compared with children with less severe disease. The same has been observed in adult groups, but it tends to favor a relationship with lower vitamin D levels, more severe radiological involvement, and increased bacterial loads.[4,7,13] There is a paucity of information in children specifically but overall tends to support a relationship between low levels of vitamin D and severe forms of the disease with more severe radiologic findings and more severe bacterial loads.

We also discovered a close association between under-nutrition and vitamin D deficiency. Children with undernutrition were more likely to have vitamin D deficiency than those with a normal BMI. This is biologically understandable, since malnutrition influences the dietary intake, absorption, and metabolism of vitamin D, and is frequently accompanied by low sunlight exposure and inflammation.[15,16] Under-nutritional factors, in combination with deficiencies of vitamin D and TB, in our group, provide grounds to embrace the idea of nutritional interventions in children with TB.

Biological plausibility: Several experimental studies support the relationship between vitamin D levels and TB outcomes. Vitamin D enhances the production of cathelicidin and other antimicrobial peptides in macrophages, thus beneficial to the killing of M. tuberculosis. <|human|>Acen et al. revealed that in active TB in adults, the levels of vitamin D are low with altered levels of cathelicidin, indicating that low levels of vitamin D may damage the effective immunity against TB.[13]

Cytokine responses also influence the ratio of Th1 to Th2 cells and the regulatory T-cell-mediated inhibition of adverse immune reactions, providing the biological basis for the observed associations in the pediatric and adult TB groups.

Supplementation trials. Evidence on supplementation trials is scarce, and existing data is limited to animal research.

The results of vitamin D supplementation studies have been mixed, although there has been strong observational and biological evidence. The efficacy of high-dose vitamin D in preventing TB was also tested in a randomized controlled trial in Mongolia, as a preventive measure for schoolchildren. Still, it was not found to significantly reduce TB infection or the disease.[14] Even among adults with active TB, there is some evidence of minimal increases in sputum conversion with healed imaging, and none of meaningful improvement in small trials.[4,7,13]

The whole idea of varying outcomes could be partly explained by differences in baseline vitamin D levels, dosing strategies, genetic factors, and the presence of existing nutritional deficiencies. Thus, our findings hint at a relationship rather than a cause-and-effect relationship and warrant further research, rather than urging high-dose vitamin D as a cure for TB.

Public health implications

India has a high TB burden, even though much progress has been made through the National TB Elimination Programme.[1,3] Vitamin D deficiency is widely spread among Indian children at the same time. Based on this scenario, our research suggests that the majority of the children with pulmonary TB either lack or have inadequate amounts of vitamin D, and the deficiencies are linked to additional serious disease, as well as under-nutrition.

Practically, these results lead to the conclusion that:

1. Regular monitoring of vitamin D levels might prove useful with TB kids, particularly Filipino kids who are undernourished or severely ill.
2. Such complications as a balanced diet, vitamin support, and safe sunlight exposure should be regarded as the main aspects of TB care.[11,12,16]
3. The target supplementation with vitamin D can also be a reasonable approach in the context of the overall nutrition recovery of children with vitamin D, with the existing pediatric practice, despite a lack of understanding of its specific effect on TB outcomes.[11,12,18]

Yet, there is no current evidence to support general high-dose vitamin D supplementation for TB prevention or treatment, so we cannot provide such approval at the moment. It should also make decisions in accordance with national and international recommendations and consider individual risk factors.[4,14]

Strengths and limitations: The strengths of the study include a prospective study design, cut-offs based on vitamin D concentrations using the IAP, and a comprehensive review of clinical, nutritional, and radiological variables in a well-defined cohort of children with pulmonary TB. Quality controls were

used to determine test results using a standard chemiluminescent immunoassay.

Several significant limitations are to be mentioned:

- There was a small sample (n=30), which restricts the accuracy of estimates and prevents the possibility of a multivariable model being robust.
- It lacked a control group of healthy children or those with different conditions of respiratory diseases. Hence, we cannot directly quantify the additional risk of low vitamin D in TB patients compared to non-TB patients.
- The study was not a direct result of considering seasonal variations in the production of vitamin D, yet the study covered several seasons.
- Being a single-center observational study, we cannot provide causality, and other residual variables such as socioeconomic status, diet, and physical activity can have an influence.
- We did not monitor the variations in 25(OH)D levels during TB treatment and any independent supplementation that the clinicians might have been administering.

Irrespective of these inadequacies, the study contributes to the paucity of pediatric studies in India and provides evidence to support the notion that low vitamin D levels are prevalent among children with TB and that the condition is associated with more severe disease.

Conclusion

This prospective study of 30 children with pulmonary tuberculosis based in this hospital showed that the majority of the children had low levels of vitamin D. Sixty percent of them were deficient, whereas 23.3 percent fell under the insufficiency category as per IAP cut-offs. A vitamin D deficiency was closely associated with under-nutrition and moderate-severe lung TB. Children with more severe disease had a lower mean serum 25(OH)D.

These results underscore the need to identify and address the problem of low vitamin D levels as a component of pediatric TB treatment. Though the present evidence does not justify the use of vitamin D supplements as an independent anti-TB measure, frequent examinations and appropriate management of the deficiency, within the framework of broader nutritional support, appear justified. Further, multicenter studies, such as an intervention trial, are required to clarify the role of vitamin D in the development of TB and its usefulness as an addition to or alternative treatment in children.

Recommendations

1. **Clinical practice:** Keep in mind the regular screening for vitamin deficiency in children with pulmonary TB. This is more so in the case of the undernourished and individuals whose lungs have much damage, as seen in X-rays.
2. **Nutritional management:** As needed to supplement normal nutrition plans, add vitamin D supplements, when necessary, to pediatric TB patients, according to IAP and national guidelines.[11,12]
3. **Research:** Carry out bigger, multicentric, controlled research to gain a greater insight into the prevalence of low vitamin D in pediatric TB. In addition, assess the effects of targeted vitamin D supplementation on clinical and microbiological outcomes.
4. **Policy:** Enhance the community health measures addressing the usual underlying causes of TB and vitamin D deficiency, like poverty, overcrowding, unhealthy eating, and inadequate access to safe outdoor locations.

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Conflicts of interest

There are no conflicts of interest.

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